Extraintestinal infections by *Escherichia coli*

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Abstract

Extra intestinal Pathogenic *Escherichia coli* (ExPEC) is a leading cause of invasive infections. These include entities like bacteremia, respiratory tract infections, meningitis and sepsis among others. Invasive ExPEC infection complicates the clinical treatment of other conditions. It is also associated with increased mortality, duration of hospital stay, and worse clinical outcomes. Older adults having comorbidities are at highest risk of acquiring these infections. ExPEC is of particular interest in the Asia-Pacific region, due to aging populations and increasing antimicrobial resistance.

Keywords: ExPEC; Bacteremia; UTI.

INTRODUCTION

Escherichia coli are a Gram negative aerobic-to facultatively anaerobic bactwrium which is known to cause diarrhoea and dysentery commonly. It sometimes constitutes the normal resident or commensal flora of the gut in humans and other warm-blooded animals. The genus *Escherichia* was described first by the German microbiologist Theodore Escherich. Though commonly associated with gut infections; it may also be implicated in extra intestinal infections. In fact, it is a major contributor of Urinary tract infections in man. These strains are hence also termed extraintestinal pathogenic *Escherichia coli*. Extraintestinal pathogenic *Escherichia coli* (ExPEC) is the commonest Gram negative bacterial pathogen seen in humans. In fact, ExPEC causes the vast majority of urinary tract infections (UTIs), and also bacteremia in adults. It is also the second most common bacterial etiological agent of neonatal meningitis.[1]

The full list of extraintestinal infections where *Escherichia coli* is incriminated is as follows:

a. Urinary tract infection: *E. coli*causes a major chunk of both community-acquired and catheter associated UTI. In fact, it alone can lead to 50-70% cases of UTI in adults. Such isolates of *E. coli* are termed UPEC or Uropathogenic *E. coli*. Midstream urine specimen is generally needed for diagnosis of UTI by microscopy and culture. Several

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virulence factors are also attributed behind causation of UTI by *E. coli*, like fimbriae, adhesins, capsule, mannose-sensitive hemaggulitinin and hemolysin. Some other virulence factors also reported commonly, are polysaccharide capsules, outer-membrane vesicles, flagella, curli, non-fimbrialadhesins, outer-membrane proteins (or OMPs) and iron-acquisition receptors. There is an overall preponderance of phylogenetic group B2 of *E. coli* among strains that cause UTI.[2] UTI is found more commonly in adult females as compared to adult males, due to factors like shorter length of perineum in females. Rising prevalence of strains that are resistant to first-line oral antimicrobial agents like trimethoprim-sulfamethoxazole, ampicillin, and fluoroquinolones are found globally among the uropathogenic *E. coli* isolates.[1]

b. Bacteremia: *E. coli* is also a leading cause of bacteremiain both adults and neonates. The most common source of suchbacteremia in adults is the urinary tract. About 2% and 6% of male patients who undergo transrectal prostate biopsy may later develop infectious complications, includin gbacteremia.[1] The overall annual incidence of *E. coli* bacteremia in adults hovers between 30 and 50 cases per 100000 populations. However, this figure increases markedly with age.

c. Neonatal meningitis: *E. coli* is one of the most important etiological agents causing meningitis is neonates (neonates are newborn babies less than 28 days of age), along with other bacteria like *Klebsiella pneumoniae*. It usually follows bacteremia due to *E. coli*. Neonatal meningitis is frequently caused by *Escherichia coli* and also others like group B streptococci.[3] NMEC (Neonatal meningitis associated *E. coli*) strains appear to mimicfecal commensal strains in terms of phylotype and serotype, butstill contain the RS218 plasmid. The latter harbours many sequences similar to those seen in UPEC. These isolates also frequently have the K1 capsule, which is a marker for neuroinvasiveness.[4]

d. Liver abscess: *Escherichia coli* have also been held responsible for the causation of pyogenic and pyaemic liver abscess. It reaches liver via portal vein and then causes multifocal abscesses there. Other bacteria may also cause liver abscess, like *Klebsiella pneumoniae* and *Enterococcus* spp. *E. coli* liver abscess reportedly has a relatively higher mortality rate. It is associated with preexisting factors like underlying malignancies, multiple abscesses and pronounced hypoproteinemia.[5] Biliary tract disease is now recognized as the commonest source of pyogenic liver abscess (PLA). Obstruction of bile flow aids in bacterial proliferation. Biliary stone disease, obstructive malignancies affecting the biliary tree, stricture, and also congenital diseases can be common triggering factors behind pyogenic liver abscess.[6]

e. Epididymorchitis: Gram negative bacterial flora of gut, like *Escherichia coli* are responsible for a large share of cases of epididymorchitis.[7]

f. Superficial abscesses like ischiorectal and perianal abscesses: *Escherichiacoli* is the predominant pathogen isolated from perianal abscesses in patients without DM (Diabetes mellitus). *Klebsiellapneumoniae*, however, has been the predominant microorganism in is chiorectal and all other abscesses in DM patients.[8] Other aerobic and anaerobic microorganisms are also responsible for these abscesses, like *Bacteroides fragilis, Peptostreptococcus,Prevotella*spp., *Fusobacterium, Porphyromonas, Clostridium* spp., *Staphylococcus aureus* and *Streptococcus* spp.[9]

g. Community acquired pneumonia: *Escherichia coli* community acquired pneumonia (CAP) is an under recognized entity which is associated with higher mortality when compared to other well studied causes of pneumonia. *E. coli* pneumonia is also frequently associated with bacteremia. Despite the absence of abdominal or urinary symptoms, the infection may originate from an occult gastrointestinal (GI) source, since *E. coli* is a common commensal resident of the GI tract. Conditions related to extra intestinal pathogenic *E. coli* (ExPEC) are garnering attention. There has also been an obvious trend towards the rise of pneumonia secondary to gram-negative

bacteria.

h. Other conditions like emphysematous pyomyositis, spontaneous meningitis, septic arthritis, and non vertebral hematogenous osteomyelitis may also be caused by *Escherichia coli*.[2] Osteomyelitis caused by *E. coli* generally affects the vertebrae or the ribs, and the source of spread is the gut and the urinary tract.[10]

Fig. 1: *E.coli urinary isolate on CLED AGAR (with Andrade indicator)*

Fig. 2: *Respiratory isolate of E. coli onMacConkey Agar*

DISCUSSION

Ways to diagnose and treat these infections early on, by ExPEC should be accorded top priority. Vaccines should be researched upon, particularly against UPEC (uropathogenic *Escherichiacoli*). Extraintestinal Pathogenic *Escherichia coli* (ExPEC) is a leading cause of invasive disease, like bacteremia and sepsis. Invasive ExPEC disease (IED) has the potential of complicating the clinical treatment of other conditions as well, and is associated with increased mortality, hospitalization, and bad clinical outcomes. Older adults and individuals with comorbid conditions are at greater risk of IED. ExPEC is of particular concern in the Asia-Pacific region due to reasons like aging population and rising antimicrobial resistance.

The technique of in vivo bioconjugation is an important advance with implications that may be as far reaching as that of the original development of conjugation technology. Bioconjugation refers to the biosynthesis of polysaccharide and carrier protein within *E. coli* strains, and then there in vivo coupling by means of the oligosaccharyltransferase PglB enzyme from the N-linked protein glycosylation system. This was originally identified in *Campylobacter jejuni* and subsequently transferred to *E. coli.*[12] In the bioconjugation procedure, PglB helps transfer diverse O polysaccharides to a protein carrier (like EPA) present in the periplasm, from which the resulting bioconjugate is then harvested by a generic purification process.[13] Thus, this bio conjugation process allows for in vivo conjugation of multiple specific O polysaccharides to specific sites of any protein carrier. It also obviates the requirement for chemical detoxification of LPS. Polysaccharide-protein conjugate molecules devised by this process have a well-defined and homogenous structure. They do not suffer from loss of epitopes, which cantake place during chemical conjugation processes.

ExPEC is a global pathogen causing a spectrum of diseases affecting all ages. The increasing incidence and associated costs of disease caused by ExPEC and the major problems associated with the emergence and spread of MDR ExPEC strains implies that an effective vaccine against ExPEC infection is of urgent need. The O antigen is a feasible vaccine target which has been shown to be immunogenic in man, with induction of opsonophagocytic antibodies shown. It has been found to conferprotection against lethal challenge in preclinical models. For the first time, the technique of bioconjugation has set up the possibility of the development of a multivalent O antigen–based bioconjugated ExPEC vaccine. It is hence desirable that an effective ExPEC vaccine may be routinely implemented in adults over 50 years of age, along with existing influenza and pneumococcal vaccine coverage in this age group.

CONCLUSION

Although intestinal colonization and infection by *E. coli* is common, various extraintestinal infections are also not very uncommonly encountered and should not be neglected by any means.

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